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Evaluation of mean platelet volume (MPV) levels in brucellosis patients

Bruselloz hastalarında ortalama trombosit hacmi (MPV) düzeylerinin değerlendirilmesi

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Abstract

Aim. Brucellosis is a multisystemic infectious disease. An inflammatory process occurs in brucellosis which causes increase in acute phase reactants. Mean platelet volume (MPV) has been shown as an inflammatory marker in some diseases. In this study we searched the MPV levels of brucellosis patients. **Method.** MPV levels of forty-seven patients with brucellosis were evaluated. **Results.** We included a total of 47 brucellosis patients having an average age of 47.4±14.6 and sex distribution of 21 (44,7%) male and 26 (55,3%) female and also 47 control healthy subjects having an average age of 45,2±12,3 and sex distribution of 25 (53,2%) male and 22 (46,8%) female). Erythrocte sedimentation rate (ESR), MPV, red cell distribution width (RDW), Hemoglobin (Hgb) and white blood cell(WBC) values in pre-treatment stage were statistically different from after treatment period. MPV levels were significantly lower in the pretreatment group. Similarly RDW values were lower in pretreatment group. MPV levels of patients were not diffrent in the acute and subacute stage. There was not any significant difference in the MPV levels of patients with hepatomegaly and without hepatomegaly (MPV levels of patients with splenomegaly were lower than patients without splenomegaly Spearman's correlation analysis showed a significant negative correlation between STAT (serum tube agglutination test) and MPV values. **Conclusion.** MPV levels may be useful in the follow-up of brucellosis patients.

Keywords: Brucellosis, acute phase reactant, mean platelet volume

Özet

Amaç. Bruselloz multisistemik bir enfeksiyon hastalığıdır. Brusellozda akut faz reaktanlarının artmasına neden olan inflamatuar bir süreç izlenmektedir. Mean platelet volume (MPV)' nin bazı hastalıklarda inflamasyonu gösteren bir değer olduğu gösterilmiştir. Bu çalışmada bruselloz hastalarının MPV düzeylerini araştırmayı amaçladık. **Yöntem.** Kırkyedi brusella hastasının MPV düzeyleri incelendi. **Bulgular.** Çalışmamıza yaş ortalaması 47,4±14,6 olan, 21 (%44,7) erkek, 26 (%55,3) kadın,toplam 47 bruselloz hastası ve yaş ortalaması 45,2±12,3 olan 25 (%53,2) erkek, 22 (%46,8) kadından oluşan 47 kişilik kontrol grubu dahil edildi. Tedavi öncesi ve tedavi sonrası eritrosit sedimentasyon hızı (ESR), MPV, red cell distribution width (RDW), hemoglobin (Hgb), beyaz küre (WBC) değerleri arasında istatistiksel olarak anlamlı farklılık mevcuttu. Tedavi öncesi MPV düzeyleri anlamlı olarak düşüktü. Benzer şekilde tedavi öncesi RDW değerlerinde de anlamlı düşüklük saptandı. Akut ve subakut faz arasında MPV düzeyleri açısından farklılık saptanmadı. Hepatomegali olan ve olmayan grupta da MPV düzeyleri açısından belirgin bir fark yoktu. Splenomegalisi olan hastaların MPV düzeyleri splenomegalisi olmayan hastalara göre daha düşük idi. Spearman korelasyonu, STAT (serum tube agglutination test) ve MPV arasında anlamlı negatif bir korelasyon gösterdi. **Sonuç.** MPV düzeyleri bruselloz hastalarının takibinde kullanışlı bir tetkik olabilir.

Anahtar sözcükler: Bruselloz, akut faz reaktanı, mean platelet volume

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Introduction

Brucellosis is a zoonosis caused by Gram-negative bacteria, Brucella spp. The disease spreads to humans by the ingestion of raw dairy products, the consumption of infected meat from domestic livestock (goats, cattle, sheep, water buffalo, camels and pigs) and close contact with their secretions and carcasses. Myalgia, high fever, and arthralgia of the large joints are the main symptoms. Brucellosis usually causes abortion and sterility in animals, while it may lead to a variety of clinical presentations, such as fever and septicemia, and even multiple organ involvement, in humans [1]. Brucella infection has been reported to cause hematologic abnormalities including anemia, leukopenia, thrombocytopenia, and clotting disorders [2, 3].

Hematological abnormalities, ranging from a fulminant state of disseminated intravascular coagulopathy to subtle hemostatic alterations have been reported in Brucella infection [4, 5]. Isolated thrombocytopenia (platelets <150x109/L) was seen in 8% of cases in a study reported from Turkey [6]. Immune-mediated thrombocytopenia may also occur during the course of brucellosis [7].

Neutrophil and platelet count are the markers that reflect the inflammatory response [8]. Mean platelet volume (MPV) is a parameter of complete blood count (CBC) analysis that is usually used by clinicians [9]. MPV correlates with the platelet function and activation [10, 11]. Previous studies have shown that MPV is a reflection of both proinflammatory and prothrombotic conditions, where thrombopoietin and numerous inflammatory cytokines (e.g. IL-1, IL-6 and TNFalpha) regulate thrombopoiesis. The intensity of systemic inflammation can be viewed as a distinctive factor for classifying conditions associated with large and small-sized circulating platelets [12]. MPV is linked to cardiometabolic risk factors such as obesity, hypercholesterolemia, diabetes, hypertension and arterial stiffness [13-17]. Moreover, several studies have shown that elevated MPV is associated with the risk of cardiovascular disease such as myocardial infarction, stroke, and peripheral artery disease [18-20]. As well as some evidence can be found through the literature about the association between the rheumatic diseases can also either decrease or increase MPV levels [12, 21, 22]. There are a few studies about MPV levels in brucellosis [23, 24]. In the present study we will evaluate the relationship between MPV, C-Reactive Protein (CRP) and ESR levels of brucellosis patients due to the stage of the disease.

Material and methods

This retrospective study was performed in 47 brucellosis patients who were admitted to the infectious diseases clinic between January 2011 and March 2013 by analyzing our hospital automation system data and a control group of 47 healthy adults were included. Age, gender and laboratory findings of these patients were investigated. Patients' complete blood counting (CBC: Leukocyte, neutrophile, lymphosite, platelet, MPV), ESR CRP values and serum tube agglutination test (STAT) results were evaluted. Fasting blood samples were taken from the participants in the morning. MPV was analysed by the Advia 120 automated blood cell counter.

Exclusion criterias of the study were:

1. History of chronic inflammatory diseases such as rheumatoid arthritis, ankylosing spondilitis.
2. Systemic diseases (hypercholesterolemia, diabetes, hypertension, arterial stiffness, myocardial infarction, stroke, and peripheral artery disease).
3. History of longterm drug usage and smoking.
4. To have an infectious disease except brucellosis.

Statystical analysis

Statistics were run with Software package STATA 11.0 (College station, Texas, USA). Continuous variables were expressed as mean ±standard deviation (SD) and categorical variables were expressed as percentage. Differences in the means of continuous variables

between 3 groups (pre-treatment, after treatment and control groups) were analysed using ANOVA (analysis of variance). Continuous variables were also compared using an independent-groups Student's t test if normality assumptions were met; otherwise, groups were compared using the Wilcoxon rank sum test. An analysis of normality of the continuous variables was performed with the Kolmogorov-Smirnov test. Spearman's test was used for correlation analyses of the parameters measured in the pretreatment period. A p-value of <0.05 was considered statistically significant.

Results

Of 47 patients with brucellosis, 21 (44.7%) were male, 26 (55.3%) were female. The mean age was 47.4±14.6 in patient population. Of 47 control cases, 25 (53.2%) were male, 22 (46.8%) were female and their mean age was 45.2±12.3. Of the 47 brucellosis cases, 35 (74.5%) was acute and 12 (25.5%) was subacute brucellosis. All patients had fever, 15 (31.9%) had hepatomegaly and 14 (29.8%) had splenomegaly. Brucella serum tube agglutination titres (STAT) were positive at a titer of 1/320 in 6 (12.8%) patients, 1/640 in 21 (44.7%) patients, 1/1280 in 18 (38.3%) patients and 1/2560 in 2 (4.3%) patients.

We determined thrombocytopenia only in one case and thrombocytosis in another case in the pre- treatment group. Laboratory parameters of brucellosis cases and control group are presented in Table 1. CRP, ESR, MPV, RDW, Hgb, WBC values in pre-treatment stage were statistically different from after treatment stage. MPV levels were significantly lower (p=0.039) in the pretreatment group. Similarly RDW values were lower in pretreatment group (p=0.035). MPV levels of patients were not different between the acute and subacute stage. (7.7±0.9 versus 7.7±0.8, p=0.956), and between patients with and without hepatomegaly (7.6±0.9 versus 7.9±0.8, p=0.351). MPV levels of patients with splenomegaly was lower than patients without splenomegaly (7.3±0.8 versus 7.8±0.9).

Spearman's correlation analysis showed a significant negative correlation between STAT and MPV values (r=-0.301, p=0.040) (Table 2). Spearman's correlation analysis of the parameters in pretreatment group did not show correlation between MPV (p>0.05), PDW (p>0.05), PLT (p>0.05), with CRP (p>0.05), ESR (p>0.05) values. There were not any correlation of STAT (p>0.05), with PDW (p>0.05), and PLT (p>0.05), values.

Table 1. Laboratory results of groups.

	Brucellosis cases		p	Controls	P (oneway ANOVA)
	Pre-treatment	After treatment			
CRP (mg/dL)	15.6±8.9	0.4±0.2	<0.001	0.3±0.1	<0.001
ESR (mm/h)	44.2±20.4	13.3±4.11	<0.001	9.3±3.8	<0.001
PLT (k/uL)	262.6±75.1	282.4±58.7	0.158	236.4±46.2	0.005
MPV(fL)	7.73±0.87	8.13±1.02	0.039	8.2±0.9	0.042
PDW (%)	16.7±2.3	17.2±0.8	0.188	16.9±0.8	0.301
RDW (%)	13.9±1.3	14.6±1.7	0.035	14.6±1.4	0.044
Hgb (k/uL)	13.3±1.6	14.0±1.3	0.033	14.1±1.5	0.038
WBC(k/uL)	7738±2432	6407±1631	0.003	6941±1191	0.026

Table 2. Spearman's correlation analysis in pretreatment group.

	MPV	PDW	PLT
CRP (mg/dL)	-0.130	-0.036	0.245
ESR (mm/h)	-0.191	-0.043	-0.242
STAT	-0.301	-0.180	-0.082

Discussion

Brucellosis is one of the great imitators in the world of infectious diseases and it can mimic various multisystem diseases, showing wide clinical polymorphism, which frequently leads to misdiagnosis and treatment delays, further increasing the complication rates [1]. Its prevalence is more than 10/100000 population in some endemic countries [25]. Clinically it may progress as a subclinical, acute, subacute or chronic infection. Since Brucella spp is an intracellular bacteria and relapse is often seen [1, 26, 27].

The diagnosis of brucellosis include clinical features, serology and culture [1, 28]. Immune-mediated thrombocytopenia may also occur during the course of brucellosis [6] And an inflammatory process occurs in brucellosiscausing increase in acute phase reactants [29, 30].

Mean platelet volume is an important indicator of platelet activation. Larger platelets contain more intense granules and are more thrombotic than normal-sized platelets. Furthermore, MPV value correlates with the degree of platelet activation and inlammatory response [31]. Several studies in the literature reported an association between MPV and chronic inlammation or infectious diseases [31]. Platelet distribution width (PDW) directly measures the variability of platelet size [32]. Platelet mass (PM), which is the indicator of total platelet mass in blood, is calculated by multiplying MPV and PLT [33]. It is not exactly clear what changes occur in platelet parameters in brucellosis. Although there are various data about hematologic effects of the brucellosis in literature, a clear pathogenesis of alteration in platelet parameters, which may be associated with morbidity in this disease, is still lacking. Infections, especially respiratory, urinary, gastrointestinal, bone and meningeal have various effects on count and functions of the thrombocytes [34, 35]. Severally studies revealed normocellularity or hypercellularity in bone marrow aspiration of patients with brucellosis [3, 36]. However, several studies reported bone marrow hypoplasia. Mild anemia and leukopenia are common in brucellosis, but isolated thrombocytopenia and pancytopenia are less common. These complications are usually associated with acute infection [3, 5, 37, 38]. As reported in literature, frequency of thrombocytopenia in brucellosis has been 1-8%, and bleeding complications have been 13-19% [2, 39]. Citak et al. [39] reported nine pancytopenia and five immune thrombocytopenia cases that were positive Brucella spp. in blood cultures in 146 children with brucellosis. Brucella grew in 50 patients blood culture and two patients' CSF culture [39]. Akbayram et al. [40] reported isolated thrombocytopenia in some patients with brucellosis, and bone morrow aspiration revealed increased megakaryopoiesis in two of these five patients and thrombocytopenia reversed with medical treatment. Isolated thrombocytopenia may occur in brucellosis even in patients with active bone marrow and is improved by medical treatment [2, 3, 5, 36-40]. But change in platelet parameters between pre and post treatment periods was not clearly explained in those studies [2, 3, 5, 36-40].

In our study we found an increment in the MPV levels of brucellosis patients after treatment. Çatal et al. [41] reported a significant correlation between urinary infection and MPV elevation. Kucukbayrak reported that postoperative MPV levels were lower than preoperative levels in patients with hydatid cyst [24]. No significant change in platelet count was determined in our study. In Kucukbayrak's another study, platelet count reduced after the treatment, but MPV was elevated. They explained this situation with splenic sequestration of big platelets in the pretreatment period characterized with active bone morrow. Kucukbayrak et al. [24] observed MPV decrement while platelet count was increased. The decrease of platelet production and splenic sequestration after the treatment may cause elevation in MPV value, so may be decreased in platelet count.

The main reason of decreased MPV in brucellosis is unclear, but during inflammatory process IL-1, IL-6, trombopoetin and cytokines play important role in regulating megakaryocyte ploidy and platelet number [42-44]. Demirbag et al. [29] reported TNF-α

and IFN-γ levels were higher in acute phase of brucellosis than control group. In Akbulut's study et al. [46] TNF-α and IL-6 levels were found to be higher in patients compared the values of posttreatment and the control group [45]. Among from these mediators, IL-6 is thought to be the major responsible factor for low MPV levels. Another possible mechanism is considered as; larger platelets which are metabolically and enzmatically more active used in inflammatory process and smaller platelets cause a decrease of MPV [47]. Ozturk et al. [23] suggested that MPV may involve in the pathophysiology of brucellosis.

In our study we could't find a correlation between MPV-CRP or MPV-ESR. Ozturk et al. [23] reported a significant negative correlation between MPV and ESR.

MPV might be a cheap and simple biomarker during follow-up of brucellosis. It may be an easy and avaible test when considered with other diagnositc tests in this disease. But, further studies are needed to establish the role of MPV in the pathogenesis of brucellosis.

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